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THE IMPACT OF VASOACTIVE DRUGS ON OXYGENATION AND TISSUE PERFUSION

Therese M. Neely, Captain, USAF, NC

1992

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University of Maryland at Baltimore

ABSTRACT

THE IMPACT OF VASOACTIVE DRUGS ON OXYGENATION AND TISSUE PERFUSION

The purpose of this paper is to discuss vasoactive drugs and how these drugs affect oxygenation and tissue perfusion. The concepts of oxygenation and tissue perfusion are assessed in terms of oxygen delivery and oxygen utilization. Oxygen delivery includes assessing arterial oxygen content, cardiac output, myocardial contractility, preload and afterload. Oxygen utilization assessment includes oxygen consumption and oxygen extraction. Both vasoconstrictive and vasodilating drugs are analyzed in terms of available research on their impact on oxygenation and tissue perfusion. Vasoconstrictive drugs, specifically dopamine, epinephrine and norepinephrine, increase preload thus enhancing cardiac output if the myocardium is strong enough to respond to the additional volume. Nitroglycerin and nitroprusside, both vasodilators, enhance cardiac output through improved forward flow. Nitroglycerin research is specific to its impact on the myocardium. Three physiological factors preventing optimal functioning of these drugs are reviewed. Included in this discussion are ventilation/perfusion mismatches, shifting of the oxyhemoglobin dissociation curve and the impact of oxygen free radicals. The forum of advanced nursing practice roles provides an opportunity to explain the use of this information in the clinical setting. The advanced nursing practice roles discussed include clinical expert, consultant, educator and researcher. These roles make up the requirements for the clinical nurse specialist.

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The Impact of Vasoactive Drugs on Oxygenation and Tissue Perfusion

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Seminar Paper submitted to the Faculty of the
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Table of Contents

CHAPTER 1

Introduction

Nurses caring for critically ill patients, either in the emergency room or intensive care setting, respond to a patient's need for oxygen on a daily basis. The goal of oxygen administration is to provide oxygen to the tissues and cells, thereby preventing anaerobic metabolism (Ahrens, 1987). Sometimes oxygen administration alone is not enough to provide the amounts needed for adequate cellular oxygenation and tissue perfusion. Pharmacological agents may be used to increase oxygen delivery to the cells through increased cardiac output. Frequently these drugs will be vasoactive drugs which constrict or dilate the blood vessels. As the drugs act, cardiac output is manipulated for optimum patient response.

The nurse must assess the patient for lack of oxygen, understanding both compensatory and decompensatory physiological responses (Ahrens, 1987, Shoemaker, 1987). The more complex concepts of cellular oxygenation requirements have become a crucial part of critical care nursing as the increased research of oxygenation needs of the critically ill is published. The nurse must understand the impact of the medications administered, not only in terms of oxygen delivery, but also in terms of oxygen

utilizatior at the cellular level. Medications that have clinically opposing impacts may be used together on the same patient because the individual responds with increased oxygen utilization. Critical care nurses must be aware of the cellular impact of vasoactive medication so that they can be a knowledgeable member of the nurse/physician collaborative team.

This paper will discuss the concepts of oxygenation and tissue perfusion and how vasoactive drugs impact these concepts to effect the patient's outcome. Oxygen delivery will be defined in terms of arterial oxygen content and cardiac output. Oxygen utilization will be defined in terms of oxygen extraction and consumption. Once these concepts are presented, the vasoactive drugs can be assessed in relation to oxygenation and tissue perfusion. Chapter two will focus on the mechanism of action and indications for three vasoconstrictive medications. Each medication, Dopamine, Epinephrine, and Norepinephrine, will also be viewed in terms of oxygenation concepts. Chapter three will accomplish the same objectives for two vasodilating medications; Nitroglycerin and Nitroprusside.

There are patients, despite any therapeutic interventions, who do not optimize oxygenation utilization. Chapter four will discuss a number of physiological factors which prevent optimal

functioning of vasoactive drugs. These include ventilation/perfusion mismatches, shifts in the oxyhemaglobin dissociation curve, and the release of oxygen free radicals.

The final chapter will apply the roles of the clinical nurse specialist (CNS) to the use of vasoactive drugs and their impact on oxygenation and tissue perfusion. How does the CNS, as a clinical expert, apply this knowledge at the bedside? What roles, as an educator, can the CNS use to expand the staff nurse's knowledge? What role does the CNS consultant have with regards to this topic? What research questions can be answered in the clinical setting? These questions will be considered in the final chapter.

CHAPTER 2

Oxygenation and Tissue Perfusion

The delivery of oxygenated blood to body tissues is important for all patients. The nurse must be aware of this need and constantly assess the patient's oxygen status through such physical signs as mental status changes and the appearance of central and/or peripheral cyanosis. There are also physical signs which allow the nurse to assess oxygen delivery. For example, usually the patient will have a normal cardiac output if the heart rate remains normal. If the heart rate increases to greater than 100 beats/minute the patient may experience a change in cardiac output (Ahrens, 1987). Nurses are aware of the importance of this type of physical assessment. However, technology used in the critical care setting allows the nurse to assess the patient's oxygenation and tissue perfusion with greater sensitivity.

The assessment of oxygen utilization is imperative for the critically ill patient. Oxygen consumption, a component of oxygen utilization, is related to oxygen delivery. A decrease in oxygen delivery brings about a decrease in oxygen consumption (Halfman-Franey & Bergstrom, 1989; Von Rueden, 1989; Ahrens, 1987). Research suggests that a reduced oxygen consumption relates to patients with a poorer prognosis. When measuring oxygen

consumption in 100 consecutive patients in a shock unit, researchers found patients with decreased oxygen consumption had an 80% mortality rate. This mortality rate was much higher than than the mortality rate of patients with a normal or elevated oxygen consumption (Wilson, Christensen & LeBlanc, 1972). This demonstrates the importance of aggressively assessing and maintaining optimum oxygen delivery and utilization patterns.

Oxygen Delivery

"The function and viability of all body tissues is dependent on an adequate supply of oxygen and other nutrients from circulating blood."(Sedlock, 1981, p14). The delivery of oxygen to the tissues is based on arterial oxygen content and cardiac output (Barone & Snyder, 1991; Mims, 1989; Von Rueden, 1989; Ayres, Schlichtig & Sterling, 1988; Ahrens, 1987). Arterial oxygen content (CaO_2) is determined by the amount of hemoglobin in the blood, the saturation of hemoglobin with oxygen, specifically in the arterial blood (SaO_2), and the partial pressure of oxygen, again in the arterial blood (PaO_2). The formula reads: $CaO_2 = (HgB \times 1.38 \times SaO_2) + PaO_2 \times 0.003$ (Barone & Snyder, 1991; West, 1990; Mims, 1989; Von Rueden, 1989).

Hemoglobin has the capacity to carry oxygen to the body tissues (Von Rueden, 1989; Ahrens, 1987; Guyton, 1986). The

saturation of hemoglobin with oxygen is about 98% (Von Rueden, 1989; Guyton, 1986). If this saturation falls below 90% a reduction in oxygen transport may occur. Saturation is reversible at the cellular level, allowing for the release of oxygen to the cells. Oxyhemoglobin affinity is affected by several clinical interventions and outcomes (Mims, 1989; Von Rueden, 1989; Ayres et al., 1988; Guyton, 1986). The important idea is that a patient requires sufficient hemoglobin to transport oxygen to the cells. A patient in hemorrhagic shock, for example, requires blood administration to optimize oxygen delivery.

The partial pressure of oxygen (PaO_2) in the arterial blood affects oxygen delivery, but only minimally. Normal PaO_2 does not automatically provide sufficient cellular oxygen because of its minimal impact and the requirement for adequate hemoglobin levels. Only a small amount of oxygen dissolves in plasma. Therefore, the delivery of oxygen with a normal PaO_2 and a normal cardiac output is about 15 milliliters of oxygen by the PaO_2 (Barone & Snyder, 1991; West, 1990; Von Rueden, 1989; Ayres et al., 1988; Ahrens, 1987). This knowledge emphasizes the previous statement that sufficient hemoglobin is needed to provide transport of oxygen to the cells.

Cardiac output comprises the second component of oxygen

delivery. Multiplying heart rate and stroke volume determines cardiac output. Stroke volume, the amount of blood ejected by the ventricle during each beat, is determined by contractility, preload and afterload. Preload and afterload will be the focus of attention when discussing the impact of vasoactive drugs on oxygen delivery.

Heart rates change as a compensatory mechanism for a change in stroke volume. If there is a decrease in stroke volume the heart rate may increase to maintain the cardiac output at a certain level. However, an increase in heart rate reduces the length of diastole, thereby reducing filling time for the heart. This can limit the amount of increase in cardiac output. An additional strain, is the increased myocardial oxygen demand brought on by the increased heart rate (Bumann & Speltz, 1989; Charette, 1989; Sedlock, 1981).

A healthy heart provides an adequate stroke volume when bradycardia occurs. An example of this concept is a marathon runner who may have a heart rate of forty beats per minute during daily activities and yet is able to maintain normal blood pressure. An acute myocardial infarction patient may not be able to provide an adequate stroke volume to compensate for bradycardia. This patient will require therapeutic intervention to maintain an

appropriate cardiac output (Bumann & Speltz, 1989; Ayres et al., 1988; Guyton, 1986; Sedlock, 1981) Bradycardia may also reduce contractility and stroke volume because the myofibrils are stretched beyond their limit with the increased filling pressure (Von Rueden, 1989; Ayres et al. 1988; Guyton, 1986).

The concepts of contractility, preload and afterload must be familiar to better understand the impact of stroke volume on oxygen delivery. Contractility is the innate ability of the myocardial muscle to contract allowing for the ejection of blood from the atria and the ventricles. An increase in myocardial contractility will increase cardiac output. This added work also increases myocardial oxygen demand. A decrease in myocardial contractility will decrease cardiac output. Myocardial contractility, although inherent, is affected by preload and afterload (Urban, 1990; Bumann & Speltz, 1989; Charette, 1989; Ayres et al., 1988; Sedlock, 1981). Contractility is measured clinically by assessing the stroke volume, right ventricular stroke work and left ventricular stroke work (Urban, 1990).

The volume of blood filling the ventricles during diastole is preload. Systemic venous circulation provides the preload for the right ventricle. Left ventricular preload is from the pulmonary venous circulation. Venous constriction and dilation affect

preload. Venous constriction will increase preload while venous dilation will decrease preload. Additionally, intravascular volume will affect both right and left ventricular preload. Patients who are on high levels of positive end expiratory pressure, or for other reasons experience a decrease in negative thoracic pressures, have a decrease in preload to the left ventricle (Urban, 1990; Bumann & Speltz, 1989; Charette, 1989; Gardner, 1989; Ayres et al., 1988). Patients with elevated right atrial pressures tend to have a weakened cardiac muscle. The weakened heart muscle cannot contract effectively causing decreased right ventricular preload (Guyton, 1986). The decrease in intrathoracic pressures causes a decrease in venous return to the heart, or a decrease in preload (Ayres et al., 1988).

Optimum preload can be determined by using the Frank-Starling Law. This law states there is relationship between the volume in the heart (preload), the stretch of the myofibril during diastole, and the strength of the contraction, to a point. Therefore, as preload increases, the myofibril stretches and contractility is increased leading to an increase in cardiac output. Because preload can be manipulated by using vasoactive drugs, an optimum preload can be determined for each patient. Clinical assessment of preload includes central venous pressure for the right ventricle

and pulmonary capillary wedge pressure for the left ventricle (Urban, 1990; Bumann & Speltz, 1989; Charette, 1989; Enger, 1989; Gardner, 1989; Ayres et al., 1988; Guyton, 1986).

The resistance the heart has to pump against during systole is referred to as afterload. Afterload also is assessed in terms of the right ventricle and left ventricle. Pulmonary vascular resistance or the integrity of the pulmonic valve and pulmonary vasculature impact right ventricular afterload. Systemic vascular resistance or the integrity of the aortic valve and the systemic vasculature impact left ventricular afterload. Vasodilation causes a decrease in resistance. Vasoconstriction brings about an increase in resistance. Increased afterload causes a decrease in stroke volume if the work is greater than left ventricular capability. Increased and decreased afterload may be from compensatory measures brought on by therapeutic interventions including pharmacological therapies (Urban, 1990; Bumann & Speltz, 1989; Gardner, 1989; Halfman-Franey & Bergstrom, 1989; Ayres et al., 1988; Guyton, 1986; Sedlock, 1981).

Oxygen delivery is readily assessed, especially with the use of currently available hemodynamic equipment. Adequate oxygen delivery allows for sufficient oxygen utilization and therefore must be assessed and therapeutic interventions accomplished

appropriately. Oxygen utilization patterns also must be assessed to ensure cellular functioning is sufficient.

Oxygen Utilization

Adequate tissue perfusion through optimal oxygen delivery does not ensure sufficient utilization at the cellular level. Therefore, once optimal oxygen delivery is provided, oxygen utilization must be assessed. Oxygen demand is based on the metabolic requirements of the body. Critically ill patients of all types require increased oxygen. Usually with increased oxygen delivery, cells will increase their oxygen consumption. Because of this concept, oxygen consumption must be optimized for each patient (Barone & Snyder, 1991; Mims, 1989; Von Rueden, 1989; Ayres et al., 1988; Shoemaker, 1987). Appropriate oxygen utilization assessment parameters include oxygen extraction and oxygen consumption, and should be frequently monitored.

Oxygen extraction rates demonstrate the balance between oxygen delivery and oxygen demand. This takes into account the oxygen delivery components previously discussed and the oxygen demand brought on by the critical situation. The formula for determining oxygen extraction is: oxygen consumption divided by oxygen transport (Mims, 1989; Ayres et al., 1988; Ahrens, 1987).

Oxygen extraction parameters provide a newer method of

assessing oxygen utilization (Ahrens, 1987). The norm for an oxygen extraction rate is between 22 - 30%. This indicates that only 22 - 30% of the oxygen delivered to the cells is normally extracted for use. During times of increased oxygen demand an increase in the oxygen extraction rates should be seen. Additionally, as cardiac output decreases, an increase in oxygen extraction will be seen. An increase in oxygen extraction compensates for reduced oxygen delivery to the cells. Decreased oxygen extraction ratios are seen with a high cardiac output, reduced demand or an inability of the cells to extract the oxygen from the oxyhemoglobin component (Von Rueden, 1989; Ayres et al., 1988; Ahrens, 1987).

Optimal oxygen consumption is the ultimate goal of enhanced oxygen delivery and oxygen utilization. Oxygen consumption values are indicative of the amount of oxygen consumed at the cellular level. This parameter can also be used to assess oxygen demand although demand is not directly measured. Oxygen consumption equals the amount of oxygen delivered to the tissues minus the amount of oxygen delivered to the right heart (Von Rueden, 1989; Ayres et al., 1988). An increase in oxygen consumption is associated with increased delivery, utilization, and demand. A decrease in oxygen consumption in a critically ill patient is

associated with patients who have a low delivery or may not be able to use the oxygen delivered. An increase in lactate levels will be seen in these patients establishing the occurrence of anaerobic metabolism. When oxygen delivery and consumption increase, the lactate levels return to baseline (Edwards,1990).

Summary

Optimum oxygen delivery and optimal oxygen consumption are linked and, in the critically ill patient, require therapeutic intervention from the nurse/physician collaborative team. Though investigators have tried to determine a prognostic level of oxygen delivery and consumption, the efforts have been futile. This critical value differs from patient to patient and from disease process to disease process (Edwards, 1990). The alert clinician understands the requirement for increased oxygen delivery and oxygen consumption, constantly assessing the impact of vasoactive drugs on these parameters, thus providing the critically ill patient with the best possible care.

CHAPTER 3

Vasoconstrictive Drugs and their Impact on Oxygenation and Tissue Perfusion

Goals of vasoconstrictive therapy include maintaining arterial pressure and optimizing cardiac output and oxygen delivery (Gilbert, Haupt, Mandanas, Huaringa & Carlson, 1986). Venoconstriction will increase preload by increasing venous return to the heart. Vasoconstriction will increase afterload, indicated by an increase in systemic vascular resistance and arterial blood pressure. An increase in afterload may impair cardiac output as it requires more work by the heart to eject the same amount of blood. If the heart cannot increase it's work, stroke volume may decrease (Bumann & Speltz, 1989; Urban, 1986). However, critically ill patients can become extremely vasodilated, thereby dropping their perfusion pressures to dangerously low levels. Vasoconstriction is used to increase perfusion pressure, to a mean arterial pressure of at least 60 mm Hg, providing enough pressure to perfuse most organs (Ayres et al., 1988). Vasoconstrictive therapy should be used after fluid loading to ensure the patient is not hypovolemic (Bumann & Speltz, 1989; Ayres et al., 1988; Gilbert et al., 1986).

Dopamine

Mechanism of Action

Dopamine, a catecholamine, is an immediate precursor of norepinephrine and will release norepinephrine from nerve-ending stores. Dopamine also directly acts on alpha adrenergic and beta adrenergic receptors as well as dopaminergic receptors. Dopamine is dose dependent, stimulating different sites causing different clinical responses with increased dosage administration. Low doses of dopamine, usually considered 1 - 2 micrograms per kilogram per minute (mcg/kg/min), stimulate the dopaminergic sites. The clinical response will be an increase in renal blood flow followed by an increase in urine output. Moderate doses of dopamine, 2 - 10 mcg/kg/min stimulate $Beta_1$ receptors causing an increase in myocardial contractility and cardiac output. Toward the upper end of this dosage a slight increase in heart rate and blood pressure also may be seen. The increase in cardiac output further enhances renal blood flow so that urine output may be augmented. Doses greater than 10 mcg/kg/min stimulate alpha adrenergic receptors causing vasoconstriction. An increase in systemic vascular resistance and mean arterial pressure are noted with these high doses. Renal blood flow can decrease concomitantly with this vasoconstriction causing a decrease in urine output (Opie, 1991;

Budny & Anderson-Drevs, 1990; Zaritsky & Chernow, 1988). Patients with pulmonary hypertension experience an increase in mean pulmonary artery pressures and hypoxic pulmonary hypertension. When pulmonary hypertension is not present, dopamine increases pulmonary blood flow (Zaritsky & Chernow, 1988).

Indications

The uses for dopamine are dose-related, therefore, low dose dopamine is administered to patients requiring an increase in renal perfusion only. Moderate doses of dopamine are given to patients who need an increase in cardiac output through enhanced myocardial contractility and heart rate. High doses of dopamine can be used to increase the integrity of the systemic vasculature especially in patients who are extremely vasodilated. This will increase the mean arterial pressure, increasing the perfusion pressure of some main organs. Some clinical situations which could benefit from dopamine administration include refractory cardiac failure, cardiogenic shock, septic shock, post cardiac surgery, and acute renal failure (Opie, 1991; Budny & Anderson-Drevs, 1990; Zaritsky & Chernow, 1988; Sedlock, 1981).

Affect on Oxygenation and Tissue Perfusion

At moderate doses, dopamine increases cardiac output through its positive inotropic action. The augmentation of cardiac output

allows for enhanced oxygen delivery. Oxygen consumption moves in a linear direction with oxygen delivery, so with healthy cellular functioning, dopamine, at moderate doses, increases oxygen consumption.

Regan and his associates (1990) studied the metabolic affects of moderate doses of dopamine on normal volunteers. Five healthy males were the subjects of this study. Each subject underwent dopamine infusions of 2, 5, and 10 mcg/kg/min for a period of 45 minutes per infusion rate. Pertinent measurements included oxygen consumption, blood pressure, and heart rate. These effects were compared to those of a D_5W solution which was infused in the same manner. The order of the two infusions was randomized.

The investigators determined that systolic blood pressure was significantly elevated during the dopamine infusion at 10 mcg/kg/min, up to 150 mm Hg. They also found diastolic pressure and heart rate were increased, though not with significance at any specific dosage. Oxygen consumption increased more when dopamine was infused as opposed to the D_5W, but only at the 10 mcg/kg/min dose (Regan et al., 1990). The increase in heart rate may increase the cardiac output in these healthy males which can account for the increase in systemic oxygen consumption.

Dopamine is not administered to healthy individuals in the

clinical setting. In 1976, Wilson, Sibbald and Jaanimagi conducted a study using twenty critically ill patients. All patients were septic with 14 of the 20 patients eventually dying. Dopamine was administered to these patients with dosage adjustments being made to optimize blood pressure, cardiac output and central venous or pulmonary wedge pressure. Dopamine administration was divided into five categories: I (no dopamine); II 2 - 5 mcg/kg/min; III 6 - 10 mcg/kg/min; IV 11 -20 mcg/kg/min; V 21 - 55 mcg/kg/min.

Results demonstrated an increase in mean arterial pressure overall by 28%. Patients had a greater increase in heart rate at higher levels of dopamine as compared to lower doses, with the average increase being only 4%. Cardiac index, which is cardiac output individualized to a patient's height and weight, started out higher than a healthy individual's cardiac index, indicating a hyperdynamic shock state. Cardiac index fell in four instances with the greatest decrease being 10%. The average increase was 19% overall. Data indicated that patients receiving 21 - 55 mcg/kg/min averaged an increase in their cardiac index of 8%. Systemic vascular resistance was also measured, indexed to the individual's height and weight. Essentially, there was no change in systemic vascular resistance index (SVRI) as the dopamine increments increased. However, data did indicate an increase in SVRI with

greater doses of dopamine, indicating vasoconstriction. At dopamine doses less than 20 mcg/kg/min the SVRI fell by an average of 3%, indicating vasodilation (Wilson, Sibbald & Jaanimagi, 1976). Oxygen utilization parameters were not assessed during data collection.

The oxygen delivery parameters measured during this study included heart rate and cardiac output. The subjects, as a whole, experienced an elevated heart rate of about 5 beats per minute. Subjects who received dopamine increases of 10 mcg/kg/min or more experienced elevations of up to 14% in heart rates while subjects who received lower dose increments experienced a decrease of 1% in their heart rate. Significant trends were not discussed for heart rate. However, statistical significance was noted when cardiac index was assessed. Increases in cardiac index averaged 19% across the different dosages of dopamine. The greatest elevation in cardiac index occurred when the patient was initially placed on dopamine. The increase in cardiac index with initial dopamine administration may be related to the positive inotropic affect of the drug. Cardiac index was enhanced with all levels of dopamine administration. Elevated cardiac index and heart rate enhance oxygen delivery. However, the death of 14 of the 20 subjects indicates that, in spite of increased oxygen delivery, oxygen

utilization was not high enough to prevent tissue death (Wilson et al., 1976). Possible reasons for oxygen delivery not increasing oxygen utilization will be discussed in a later chapter.

Shoemaker et al. (1989) completed a study comparing dopamine with dobutamine while assessing the hemodynamic effects and oxygen transport parameters. Critically ill patients were given both drugs in a random order. Drugs were increased by increments of 2.5 mcg/kg/min every 20 to 30 minutes. Data measurements included oxygen delivery, oxygen consumption, and oxygen extraction. Other data obtained included cardiac index and SVRI.

The data obtained for the administration of dopamine indicated beta adrenergic receptor stimulation up to and including 7.5 mcg/kg/min. Alpha adrenergic receptor stimulation may begin at 10 mcg/kg/min. Oxygen delivery increased from 518 ml/min/sqm at baseline to 630 ml/min/sqm at 7.5 mcg/kg/min. Oxygen consumption increased in correspondence with oxygen delivery from 136 ml/min/sqm to 143 ml/min/sqm. With the increase in oxygen delivery there is a decrease in the accompanying oxygen extraction, 28.2% to 23.8%. At 10 mcg/kg/min there was an increase in SVRI, from 1654 to 1662 dynes/cm^5/sqm. The increase in SVRI was thought to indicate the beginning of alpha adrenergic recepts stimulation and vasoconstriction. Oxygen delivery decreased to 611 ml/min/sqm;

oxygen consumption decreased to 136 ml/min/sqm and oxygen extraction had a slight increase to 23.9% (Shoemaker et al., 1989).

These data support the theory that an increase in oxygen delivery is accompanied by an increase in oxygen consumption and a decrease in oxygen extraction. At higher levels of dopamine, where vasoconstriction becomes a risk, a decrease in delivery and consumption is noted. The decrease in oxygen delivery and consumption is of clinical significance as the goal of the nurse/physician collaborative team is to optimize tissue perfusion and oxygen utilization. Patients with hearts that are not strong enough to overcome the increased afterload may require decreased dopamine dosages, another inotropic medication in addition to the vasoconstricting dosages of dopamine or other therapeutic interventions.

Dopamine is a useful medication in specific settings. The nurse must constantly assess the patient's hemodynamic patterns and oxygen transport and consumption efforts to ensure the interventions remain therapeutic. Individual patients respond differently to each medication and to each dose. The nurse should not assume all patients will have dopaminergic and beta adrenergic stimulation alone up to 10 mcg/kg/min. Some patients may respond with alpha adrenergic receptor stimulation at 5 mcg/kg/min. The

astute nurse will assess and notify the physician so therapeutic adjustments can be made.

Epinephrine

Mechanism of Action

Epinephrine or adrenalin is an endogenous hormone readily released in the body during times of stress. Epinephrine at doses of 0.005 to 0.02 mcg/kg/min stimulates $Beta_1$ adrenergic receptors causing an increase in myocardial contractility, heart rate, automaticity, and cardiac conduction velocity. It is important to note that the increase in work of the heart also increases the need for myocardial oxygen. This need is not usually met with the increased cardiac output seen at low doses of epinephrine.

$Beta_2$ receptors also are stimulated at low doses causing peripheral vasodilation and bronchodilation. Hemodynamic effects of beta adrenergic stimulation include a decrease in systemic and pulmonary vascular resistance, an increase in stroke volume, left ventricular stroke work and cardiac output. Increased infusion rates stimulate alpha adrenergic receptors causing vasoconstriction and increasing systemic vascular resistance and arterial blood pressure. Venous return to the heart also is increased. Elevated venous return to the heart may increase the left ventricular end diastolic volume which augments the cardiac output as long as the

heart maintains its ability to eject blood against the elevated afterload (Opie, 1991; Ayres et al., 1988; Hancock & Eberhard, 1988; Zaritsky & Chernow, 1988). Epinephrine will constrict renal arteries at very low doses. Constricted renal arteries cause a decrease in urine output and limits the usefulness of epinephrine in patients with shock. Patients with low cardiac outputs may respond with an increased urine output as the kidney responds to an increased renal blood flow brought on by the increased cardiac output (Zaritsky & Chernow, 1988).

Indications

Epinephrine can be used for acute asthma and in the case of anaphylaxis as it has bronchodilating properties. $Beta_1$ stimulation increases heart rate and myocardial contractility making it useful in patients with low cardiac output refractory to fluid challenges and other inotropic agents including dobutamine and dopamine (Ayres et al., 1988; Zaritsky & Chernow, 1988). Epinephrine also is used in cardiac arrest situations as it increases systemic vascular resistance, arterial blood pressure, heart rate, coronary and cerebral perfusion pressure, myocardial contraction and automaticity brought on by the mixed alpha and beta adrenergic receptor stimulation (American Heart Association, 1987). Epinephine, at higher doses, will constrict renal and cutaneous

vascular beds. Constriction of renal and cutaneous vascular beds elevated mean arterial pressure as well as afterload. Skeletal muscle, coronary and cerebral blood flow as well as visceral blood flow may increase with the increased cardiac output induced by the inotropic and chronotropic action on the heart. The actions of epinephrine indicate that beta stimulation is more powerful than the alpha stimulation also experienced (Ayres et al., 1988). Disease processes which respond to appropriate epinephrine administration include acute asthma, cardiogenic, anaphylactic, and septic shock, and cardiac arrest (Zaritsky & Eisenberg, 1986).

Affect on Oxygenation and Tissue Perfusion

Epinephrine, as with dopamine, has inotropic properties that impact on oxygen delivery. Additionally, it increases heart rate which also enhances cardiac output. As administration dosages increase, epinephrine demonstrates a stimulation of alpha adrenergic receptors which will assist in increasing blood pressure to a limited extent. With increased vasoconstriction an increase in afterload will be seen. If the heart cannot effectively pump against the added pressure, oxygen delivery will decrease.

A study was done to determine the metabolic and circulatory effects of epinephrine on the healthy man (Fellows, Bennett & MacDonald, 1985). Seven healthy males were used as subjects. On

three separate occasions, one week apart, epinephrine was administered for thirty minutes. Three different infusions were used. One infusion was a control, containing no epinephrine; one infusion was at 50 nanograms per kilogram per minute (ng/kg/min); and one was at 10 ng/kg/min. The infusions were performed in random order. Measurements obtained during the experiment protocol included but were not limited to: blood flow in the left hand and right calf, arterial blood pressure, heart rate and oxygen consumption (Fellows et al., 1985).

The results of this study indicated an increase in heart rate, an increase in calf blood flow and calf vascular resistance decreased, and a decrease blood flow to the hand in some subjects with an increase in blood flow in others. There was also an increase in systolic blood pressure during the high doses of epinephrine while there was a decrease in diastolic blood pressure during both levels of epinephrine administration. The researchers believed the reduced diastolic blood pressure experienced during the administration of lower doses may have masked any increase in systolic blood pressure. They also concluded that the increase in systolic blood pressure may have been linked to an increase in cardiac output. Cardiac outputs were not reported in the study. A significant increase in metabolic rate was noted, as measured by

oxygen consumption (Fellows et al., 1985).

This study of young healthy men demonstrates the mixed impact of epinephrine on the body. Both beta and alpha adrenergic receptors are stimulated, providing a mix of increased contractility and vasoconstriction which mainly occurs in the peripheral and renal beds. Heart rate increases, accompanied by enhanced contractility, will supplement the cardiac output. Oxygen consumption will increase linearly with oxygen transport. The linear correlation of oxygen consumption and transport was indicated by the enhanced metabolic rate. There was an elevation in systolic blood pressure during the high doses of epinephrine brought on by the alpha adrenergic receptor stimulation. However, in healthy males, the myocardium is strong enough to overcome the increased afterload and benefit from the increased preload.

A study was done assessing the hemodynamic and oxygen metabolism status of critically ill patients who received epinephrine. A convenience sample of 13 patients with septic shock was used. Epinephrine was the third therapeutic intervention employed, the first being volume expansion and the second being the use of dopamine. The starting dose of epinephrine was 0.05 mcg/kg/min. Infusion rates were increased to 1 mcg/kg/min at 30 minutes if systolic blood pressure was less than 90 mm Hg. Data

were collected prior to initiation of epinephrine therapy and one hour after epinephrine was started. Pertinent measurements included heart rate, cardiac index, SVRI, oxygen delivery, oxygen consumption, oxygen extraction and left ventricular stroke work index (LVSWI) which indicates the heart's ability to contract against afterload (Bollaert, Bauer, Audibert, Lambert & Larcan, 1990). Myocardial depression often is seen in septic shock patients and will affect the patient's ability to overcome an increase in SVRI brought on by any alpha adrenergic stimulation.

An increase in cardiac index, oxygen delivery and oxygen consumption were noted one hour after the epinephrine was started. Oxygen extraction decreased with the increased oxygen delivery. Patients also experienced an increase in SVRI and an increase in LVSWI from baseline. The increase in SVRI was indicative of vasoconstriction brought on by alpha adrenergic receptors. The increase in LVSWI, though not back to normal, indicated an improved left ventricular contractility. This aids in overcoming the increased afterload allowing for an increase in cardiac output (Bollaert et al., 1990).

Epinephrine provides enhanced oxygen delivery which allows for an increase in oxygen consumption. Elevated oxygen delivery is accomplished through the stimulation of both alpha and beta

adrenergic receptors. The nurse must thoroughly assess the patient's oxygenation and perfusion parameters as changes in epinephrine infusion rates are made. Each patient must be viewed as an individual with specific needs. An assessment of all the data allows for informed, comprehensive decisions to be made regarding the use of epinephrine for patients with an accumulating oxygen debt.

Norepinephrine

Mechanism of Action

Norepinephrine is a neurotransmitter and is a precursor of epinephrine. It has the ability to stimulate both alpha adrenergic and $Beta_1$ adrenergic receptors. Low doses of norepinephrine affect the $Beta_1$ receptors bringing about an increase in myocardial contractility, conduction velocity and heart rate. Low doses of norepinephrine will affect peripheral vascular resistance minimally. However, at higher doses there is a greater alpha adrenergic stimulation causing vasoconstriction. Vasoconstriction causes an increase in SVRI. This increase in SVRI indicates an elevation in afterload. An elevated afterload brings about an increase in preload. If the myocardium is healthy enough to withstand the additional volume, a further enhancement of myocardial contractility, myocardial work and stroke volume occurs.

An unhealthy heart may not withstand the increase in volume and a decrease in cardiac output and therefore oxygen delivery may occur. The heart rate decreases as a response to the increased blood pressure at higher norepinephrine doses (Ayres et al., 1988; Hancock & Eberhard, 1988; Zaritsky & Chernow, 1988).

Indications

Because of its potent vasoconstrictor properties, the usefulness of norepinephrine with critically ill patients is limited. Most often it is used to enhance perfusion pressures in patients who are dangerously vasodilated. This acute hypotension should be refractory to expansion and other therapeutic interventions before norepinephrine is used. Norepinephrine also causes vasoconstriction in the renal vasculature. This will decrease renal blood flow leading to a decreased urine output. An initial rate of 2 mcg/kg/min is frequently used and then titrated up or down to achieve the desired balance of effects. Disease processes which may respond to norepinephrine administration include cardiogenic shock and septic shock (Ayres et al., 1988; Zaritsky & Chernow, 1988).

Affect on Oxygenation and Tissue Perfusion

The main goal of norepinephrine administration is to increase oxygen delivery by enhancing perfusion pressure (Desjars, Pinaud,

Potel, Tasseau & Touze, 1987). Norepinephrine is usually used after volume expansion, inotropic support and other less potent vasopressors are tried. A study was conducted using 12 patients with septic shock. Dopamine infusion rates were kept constant at 15 + or - 2 mcg/kg/min. Hemodynamic measurements were taken three times during a control period prior to norepinephrine being infused. Beginning infusion rates were 0.5 mcg/kg/min. Hemodynamic measurements were obtained 20 minutes after initiation. Norepinephrine was increased up to 1 mcg/kg/min to increase arterial blood pressure. Repeat measurements were taken 20 minutes after the infusion was titrated up (Desjars et al., 1987).

During the 0.5 mcg/kg/min norepinephrine infusion, mean arterial pressure and SVRI increased significantly. Heart rate decreased significantly and cardiac index was unchanged. Urine output increased to more than 0.5 ml/min. The control was less than 0.5 ml/min (Desjars et al., 1987).

Hemodynamic parameters obtained for the dosage of 1 mcg/kg/min demonstrated a greater increase in mean arterial pressure and systemic vascular resistance index. Cardiac index did not decrease in four of the five patients who required the higher dosage. Urine flow did not increase at the higher dosage (Desjars et al., 1987).

This study indicated that norepinephrine increased perfusion

pressure which provided an increase in urine output. However, cardiac index did not increase significantly and heart rate decreased. The combined effect on cardiac index and heart rate indicated that oxygen delivery may have decreased or remained constant with oxygen consumption linearly following oxygen delivery. Oxygen consumption studies for these subjects might have provided this needed data.

In 1988 a study was conducted using ten patients in septic shock. They were given norepinephrine infusions after volume expansion and other inotropes and vasopressors were unsuccessful. Hemodynamic measurements were obtained including oxygen delivery and consumption values. Norepinephrine was initiated at 0.01 mcg/kg/min and increased until a mean arterial pressure of 85 mm Hg and urine output of greater than 60 ml/hour were obtained. After these results were stable for 15 minutes, hemodynamic measurements were again assessed (Meadows, Edwards, Wilkens & Nightengale, 1988).

As expected, there were significant increases in mean arterial pressure, urine output, LVSWI and SVRI. Heart rate changes were not significant and cardiac index changes were variable among patient population. Oxygen delivery and oxygen consumption parameters were measured in six subjects with varied results.

Oxygen delivery decreased with a decrease in cardiac index. An increase in oxygen delivery brought about an increase in oxygen consumption. Two of these patients experienced enhanced oxygen delivery and consumption while receiving norepinephrine. Four subjects experienced a decrease in oxygen delivery. Two of these patients had an accompanying decrease in oxygen consumption while two experienced an elevation in oxygen consumption. Trends for oxygen delivery and consumption could not be predicted. Meadows et al. (1988, p. 665) stated "we would use the results of this study to re-emphasize the unpredictability of the response to catecholamines in septic shock."

Norepinephrine is used in septic shock as a vasoconstrictor to enhance perfusion pressure. Norepinephrine has inotropic effects as well as vasoconstriction, both of which can enhance oxygen delivery. This study demonstrated the different responses an individual may have to norepinephrine.

A corroborating study was conducted in 1989 by Hesselnik and Brodin. They used five subjects who were experiencing hyperdynamic septic shock. Patients were kept on their current regimen of dopamine at rates of 7 to 20 mcg/kg/min. Dopamine, at 7 to 14 mcg/kg/min, was added to three patients' care protocols. Hemodynamic measurements and metabolic measurements were obtained

prior to the initiation of norepinephrine and one hour after the dosage had been stabilized for a systolic BP > 100 mm Hg and an acceptable urine flow. If the urine output remained unacceptable, norepinephrine was titrated for a systolic BP of up to 140 mm Hg. The range of norepinephrine doses was 0.03 to 0.5 mcg/kg/min.

The results were similar to those of Meadows and colleagues (1988). Significant increases in arterial pressure, urine output and SVRI were noted. There were no significant changes in heart rate and cardiac index. Five of seven patients experienced a decrease in oxygen delivery with four of these patients experiencing a drop in oxygen consumption (Hesselvik & Brodin, 1989).

This study provided further evidence that as oxygen delivery decreases so does oxygen consumption. However, a variable response was noted with one patient experiencing an increase in oxygen consumption when oxygen delivery has decreased. Norepinephrine is a potent vasoconstrictor and must be administered with careful attention and frequent assessments. Although oxygen delivery and consumption appear to decrease with norepinephrine administration, norepinephrine is useful for increasing perfusion pressures. Additionally, clinical studies of norepinephrine frequently assess norepinephrine in conjunction with other therapies, specifically

inotropic therapy. The impact of adjunctive therapies on the data must also be considered.

Summary

Dopamine, epinephrine, and norepinephrine each have mixed alpha and beta adrenergic effects on the body. These drugs are dose dependent and can bring about a variety of compensatory mechanisms and responses within the body. Their main use as vasoconstrictors is for people who are vasodilated and experiencing a dangerously low blood pressure. It must be remembered that therapeutic interventions used to support one function may bring about detrimental effects in another area of the body (Ayres et al., 1988).

These drugs can impact oxygen delivery by increasing preload which leads to an increased cardiac output, if the myocardium is strong enough to handle the additional volume. These drugs also have a positive impact on cardiac contractility, which will increase the force ejection, increasing cardiac output and allowing the heart to overcome any increased afterload caused by vasoconstriction. As oxygen delivery increases, oxygen consumption increases.

The research studies discussed were clinical in nature and had very few subjects. There is room on the research agenda for

further clinical research to assess oxygen delivery and consumption patterns brought on by dopamine, epinephrine and norepinephrine use. The data presented demonstrated the need for each patient to be assessed as an individual. The nurse/physician collaborative team should anticipate the patient's response to these therapies. Frequent assessment of oxygen delivery and consumption patterns must be made. The patient must receive individualized care to optimize the use of dopamine, epinephrine and norepinephrine with regards to oxygen delivery and consumption.

CHAPTER 4

Vasodilating Drugs and Their Impact on Oxygenation and Tissue Perfusion

Vasodilators have a useful role in reducing hypertension through expansion of the vascular beds. Vasodilators may dilate the venous or arterial beds or they may act on both vascular beds providing systemic vascular dilation. A goal of arterial dilation therapy is to reduce afterload. This reduces systemic vascular resistance, decreasing the work load of the heart and reducing myocardial oxygen need. Venodilation decreases preload through a reduction in venous return to the heart. Venodilators are useful when patients have excessive preload and an inability of the heart to respond to the additional work. By decreasing preload, the myocardium can contract more efficiently which will decrease any accumulated pulmonary congestion, increase stroke volume and result in an increased cardiac output. Vasodilators can also increase coronary perfusion which increases oxygen delivery to the myocardium (Bumann & Speltz, 1989; Hancock & Eberhard, 1988; Parrillo, 1988; Urban, 1986; Ribner et. al., 1982).

Nitroglycerin

Mechanism of Action

Nitroglycerin acts on vascular smooth muscle causing dilation

of the vascular bed. Low doses of intravenous nitroglycerin, 10 mcg/min - 100 mcg/min, dilate the venous bed bringing about venous pooling of the blood and a reduction in preload. Higher doses of intravenous nitroglycerin, 400 mcg/min to as high as 1000 mcg/min, act on the arterial and venous beds thereby reducing both preload and afterload. The action of nitroglycerin is more significant on the capacitance vessels. Therefore, nitroglycerin is considered a venodilator. Nitroglycerin also reduces coronary artery vasoconstriction providing an increase in coronary perfusion (Opie, 1991; Walker & Geniton, 1989; Hancock & Eberhard, 1988; Parrillo, 1988; Ribner, et. al., 1982).

Because decreases in both preload and afterload can be seen in patients receiving nitroglycerin, a reduction in left ventricular filling pressure, right arterial pressure, central venous pressure, mean arterial pressure, and systemic vascular resistance also are seen. Myocardial perfusion is enhanced by the increased cardiac output and coronary artery vasodilation. Cardiac output increases are related to the decrease in systemic vascular resistance (Walker & Geniton, 1989; Hancock & Eberhard, 1988; Parrillo, 1988). If cardiac output has not increased, the dosage being administered may be insufficient to reduce afterload (Parrillo, 1988). At lower doses, 10 -100 mcg/min, heart rate is usually unaffected but at

higher doses a slight increase may be seen in compensation for the decreased mean arterial pressure. Because of the overall reduced work load on the heart, a decrease in myocardial oxygen consumption is seen (Ardehali & Ports, 1990; Walker & Geniton, 1989; Hancock & Eberhard, 1988; Parrillo, 1988).

Indications

Nitroglycerin is useful with patients who require a decreased preload and afterload as well as an increase in myocardial perfusion. Patients who require a reduction in myocardial oxygen demand also benefit from nitroglycerin. Nitroglycerin may also benefit patients with low cardiac output accompanied by high left ventricular filling pressures and an elevated systemic vascular resistance. Disease processes which respond to nitroglycerin administration include congestive heart failure, unstable angina pectoris, acute myocardial infarction with decreased ventricular function and pulmonary edema associated with left ventricular dysfunction. Nitroglycerin therapy provides controlled hypotension, which may be required in the clinical setting (Opie, 1991; Ardehali & Ports, 1990; Walker & Geniton, 1989; Parrillo, 1988).

Affect on Oxygenation and Tissue Perfusion

Affects of nitroglycerin can be divided into two categories

both of which are discussed in the literature. The categories are systemic affects and affects on the myocardium. Systemically, nitroglycerin lowers the mean systemic arterial pressure, systemic vascular resistance and left ventricular filling pressures or preload. Stroke volume and cardiac output are increased with nitroglycerin use (Franciosa, Blank & Cohn, 1978). As previously discussed, a reduction in afterload augments cardiac output which increases oxygen delivery.

A study was done to compare intravenous nitroglycerin with intravenous nitroprusside on acute hypertension following coronary artery bypass surgery (Flaherty, Magee, Gardner, Potter & MacAllistar, 1982). The sample consisted of 17 patients who underwent coronary artery bypass grafting. Control measurements were taken upon the development of acute hypertension and prior to medication administration. The hemodynamic measurements included heart rate, cardiac output, mean arterial pressure, pulmonary capillary wedge pressure, mean pulmonary artery pressure, stroke work index, systemic vascular resistance index, pulmonary vascular resistance index, and stroke volume index. Patients were randomly assigned to one of two medication protocols, either the sodium nitroprusside first with cross over to nitroglycerin or the opposite. The infusions were started at 5-10 mcg/min and increased

every 3-5 min until the patients' mean arterial pressure was lowered 10-40 mm Hg, depending on the starting value. Stabilization occurred for 20 minutes and then cardiac outputs were re-measured to obtain a new hemodynamic profile. The first drug was discontinued and the second vasodilator was administered. The steps were repeated. Whole blood was administered to replace surgical blood loss which negated any preload lowering effects.

During nitroglycerin therapy arterial pressure decreased rapidly with an accompanying decrease in systemic vascular resistance index. Cardiac output, heart rate, and stroke volume index all increased. Mean PaO_2 and PvO_2 decreased with nitroglycerin infusion while myocardial oxygen consumption increased (Flaherty et al., 1982). This study indicates the systemic benefits which can be obtained through the administration of nitroglycerin to acute hypertensive patients.

Nitroglycerin also benefits the myocardium specifically and is most frequently used for this impact. As indicated by Flaherty and his fellow researchers (1982), myocardial oxygen consumption increased with nitroglycerin administration. A study using 14 men with angina was done to measure myocardial oxygen demand and supply during exercise before and after intravenous nitroglycerin administration (Choong et al., 1989). These men all had positive

exercise electrocardiograms. Symptom-limited bicycling was the exercise used in this study. Heart rate, radial artery pressure, and pulmonary artery pressure were continuously measured. Other hemodynamic measurements were taken intermittently, and included cardiac output, stroke volume, left ventricular stroke work, and systemic vascular resistance. Oxygen saturations and hemoglobin concentrations were obtained allowing for calculation of the arteriovenous oxygen content difference and oxygen consumption. Nitroglycerin was administered intravenously to produce a 20 mm Hg fall in mean arterial pressure while the patient was at rest. This infusion rate was maintained throughout the exercise period. A comparison between nitroglycerin and nifedipine was done during this research although only nitroglycerin results will be reported here (Choong et al., 1989).

Nitroglycerin brought about a decreased mean arterial pressure and an increased heart rate, at rest. Nitroglycerin also reduced pulmonary wedge and right arterial pressures as well as stroke volume index while cardiac index went unchanged. At maximum exercise, nitroglycerin increased the myocardial oxygen consumption while increasing the cardiac index, though not to a statistically significant degree. ST segment depression and pain were decreased during the nitroglycerin infusion indicating less myocardial

ischemia (Choong et al., 1989)

A number of mechanisms could have been utilized to bring about this decrease in ischemic events. Nitroglycerin can dilate coronary arteries which are stenosed, thereby increasing blood flow and oxygen delivery and increasing oxygen consumption (Rutherford, 1989). Nitroglycerin also maintains the coronary perfusion gradient allowing for improved blood flow to ischemic areas (Choong et al., 1989). This again increases oxygen delivery which enhances oxygen consumption.

The responses to nitroglycerin discussed here are exiting and have important clinical implications. However, it cannot be overlooked that the desired end result is increased tissue perfusion and oxygenation. Nitroglycerin should not be administered without hemodynamic monitoring as both drug tolerance and hemodynamic resistance have been reported in the literature (Packer, Medina, Yushak & Lee, 1986; Parker, Fung, Ruggirello & Stone, 1983).

A study was conducted in 1991 assessing the patient resistance to nitroglycerin therapy and to determine an alternate drug therapy which would restore vascular responsiveness to nitroglycerin. Though the findings of this study are beyond the scope of this paper, it is important to note that 10 of 26 patients used in this

study did not respond to nitroglycerin (Varriale, David & Chryssos, 1991).

This study emphasizes the importance of assessing the drug's effect on the individual. The best outcome for the patient must be determined and appropriate drug dosages must be administered to obtain that outcome. Hemodynamic monitoring using the concepts of oxygen delivery and utilization provide the optimal assessment of drug effectiveness for the patient.

Nitroprusside

Mechanism of Action

Nitroprusside acts directly on smooth muscle in the vasculature bringing about both venous and arterial vasodilation. Vasodilation decreases both preload and afterload (Opie, 1991; Walker & Geniton, 1989; Ayres et al., 1988; Parrillo, 1988). This action provides a decrease in both systemic and pulmonary vascular resistance. Nitroprusside will increase stroke volume and cardiac output especially in patients with severe heart failure. The patient's heart rate usually remains unchanged or may decrease slightly as will blood pressure (Parrillo, 1988). A greater decrease in mean arterial blood pressure is seen with higher dosages (Opie, 1991; Walker & Geniton, 1989).

An improvement in left ventricular function is seen, often

associated with the decreased ventricular impedance. Increased tissue perfusion associated with increased cardiac output also are noted. Patients with low cardiac outputs and high systemic vascular resistance benefit from nitroprusside administration (Parrillo, 1988; American Heart Association, 1987).

Indications

Patients receiving nitroprusside may experience a decrease in systemic and pulmonary vascular resistance brought on by arterial and venous vasodilation. More efficient pumping action of the left ventricle enhances cardiac output. Hypertension related to cardiac or vascular surgery or any other acute hypertensive emergency may respond to nitroprusside therapy. This vasodilator is also useful in the management of congestive heart failure, cardiogenic pulmonary edema, mitral or aortic regurgitation and persistent chest pain accompanied by hypertension (Walker & Geniton, 1989; Parrillo, 1988).

Affects on Oxygenation and Tissue Perfusion

Nitroprusside acts to increase cardiac output through a decrease in systemic vascular resistance. This allows for greater forward flow. The decrease in left ventricular impedance through the vasodilating effects of nitroprusside has the added benefit of reducing myocardial oxygen demand (Halfman-Franey & Bergstrom,

1989; Rutherford, 1989).

Flaherty and his associates (1991) described the systemic effects of nitroprusside in their research comparing nitroprusside with nitroglycerin (methods previously described). They found nitroprusside to decrease arterial pressure, systemic vascular resistance index, and pulmonary vascular resistance index. Cardiac output increased slightly with nitroprusside administration. The alveolar-arterial oxygen gradient increased, accompanied by an increase in intra-pulmonary shunting.

Although Flaherty and his fellow researchers (1991) acknowledged only slight improvements in cardiac output, other sources indicate an increase in cardiac output. This increase occurs especially when nitroprusside is administered to patients with a depressed cardiac output (Ribner et al., 1982; Lukes, Romero & Resnekov, 1979; Mookherjee, Keighley, Warner, Bowser & Obeid, 1977; Cohn, 1973).

Mookherjee and his associates (1977) assessed hemodynamic, ventilatory and blood gas changes during the administration of nitroprusside. The 16 subjects used in this study had chronic congestive heart failure. After placement of monitoring devices, control measurements were taken. Then, nitroprusside was started at 10 mcg/min. The dosage was increased every five minutes by 5 to

10 mcg until a 10% reduction in mean arterial pressure occurred or pulmonary artery pressures decreased at least 20% or both occurred. Dosages ranged from 30 mcg/min to 130 mcg/min. When stabilization had taken place for 15 minutes, hemodynamic parameters were again measured. These included heart rate, mean arterial pressure, pulmonary artery pressure and cardiac index. Calculated parameters included systemic and pulmonary vascular resistance. Expired gas was analyzed for oxygen and carbon dioxide concentration and oxygen uptake. The ratio of venous admixture to total blood flow was also evaluated.

Results from this study indicated that mean arterial and pulmonary arterial pressures decreased as did systemic and pulmonary vascular resistance when nitroprusside was administered. Cardiac index increased while the heart rate did not undergo a significant change during the nitroprusside infusion. The administration of nitroprusside did not change oxygen uptake, however, there was a significant decrease in PaO_2 (Mookerjee et al., 1977).

Mookerjee and his colleagues (1977) found nitroprusside improved hemodynamic status overall but were concerned about the significant decrease in PaO_2. They believed that nitroprusside dilated the vessels surrounding poorly ventilated alveoli, an area

which is normally vasoconstricted. This dilation of the vessels increased the blood flow through unoxygenated alveoli and decreased the arterial oxygen tension (Mookerjee et al., 1977). Other studies document this inhibition of hypoxic pulmonary vasoconstriction by vasodilators (Mollhoff, Rosiers & Van Aken, 1990; Mollhoff, Van Aken, Mulier, Muller & Lauwers, 1990).

As indicated in the discussion on oxygen delivery, PaO_2 adds minimally to the effects of oxygen delivery by arterial blood (Barone & Snyder, 1991; Von Rueden, 1989; Ahrens, 1987). However, if it is known that a drug can decrease PaO_2, then it becomes imperative for the nurse/physician collaborative team to monitor the hemodynamic status of the patient as well as the hemoglobin level. A patient who has a drug-induced decrease in PaO_2 accompanied by a low cardiac output or a low hemoglobin can experience decreased oxygen delivery and decreased oxygen consumption.

A second reason to assess oxygen delivery and utilization parameters is the varying degrees of response seen in patients receiving nitroprusside. To examine this effect, 21 patients with severe congestive heart failure were used as subjects for a study conducted by Lukes and his associates (1979). Hemodynamic measurements were obtained including pulmonary capillary wedge

pressure, cardiac output, mean arterial pressure, right atrial pressure, stroke volume index, systemic vascular resistance and left ventricular stroke work index. Nitroprusside was then initiated, beginning with 0.5 mcg/kg/min and increased until a fall in blood pressure occurred. Measurements were taken and the nitroprusside was titrated for an optimal cardiac output without risking perfusion pressures.

Of the 21 patients used in this study, 13 demonstrated hemodynamic and clinical benefits. These included increased urine output, lowering of indirect left ventricular filling pressure, enhanced stroke volume and an increased cardiac index without tachycardia or hypertension. Systemic vascular resistance decreased by 50 percent or more (Lukes et al., 1979).

On eight occasions nitroprusside was discontinued because enhanced cardiac output could not be achieved without compromising arterial pressure. On 7 occasions, a brief increase in cardiac output was followed by a reduced blood pressure. Six patients had a drop in cardiac output. As a group, the results indicated no change in cardiac output, systemic vascular resistance, stroke volume and stroke work index while both blood pressure and pulmonary capillary wedge pressures decreased. Additionally some patients required dopamine for blood pressure enhancement even

after the nitroprusside infusion was stopped (Lukes et al., 1979).

This study demonstrates the importance of assessing the end result, that of oxygen delivery and oxygen consumption, in these critically ill patients. There are patients who will surprise the nurse/physician collaborative team by responding to these medications in ways other than those documented through research. These studies provide data which encourages further research.

Summary

Nitroglycerin reduces preload by dilating the venous capacitance vessels. It also acts on coronary arteries, dilating them, and allowing improved blood flow to ischemic myocardium (Rutherford, 1989). The dilation of coronary arteries increases oxygen delivery to the heart, enhancing oxygen consumption thereby meeting oxygen demand. When used with deteriorating myocardium, nitroglycerin improves cardiac output by decreasing the volume needed to be ejected. This decrease in volume enhances left ventricular function allowing for an increase in cardiac output (Parrillo, 1988).

Nitroprusside reduces preload by dilating venous beds. Nitroprusside also reduces afterload by dilating arterial beds. An increase in cardiac output occurs because there is a reduction in left ventricular impedance, thus improving forward flow

(Rutherford, 1989). Nitroprusside also alleviates increased preload associated with left ventricular pump failure either through weakening myocardium or an incompetent valve. The decrease in volume, combined with the decreased resistance, improves left ventricular function and augments cardiac output (Parrillo, 1988). Enhanced cardiac output increases oxygen delivery to the body, allowing for an increase in oxygen consumption in these critically ill patients.

The research presented was limited in terms of the impact of these drugs on oxygenation and tissue perfusion. Nitroglycerin studies focused on myocardium oxygen delivery and consumption as nitroglycerin is most frequently used for cardiac patients. Nitroprusside studies assessed the effect of nitroprusside on hypoxic pulmonary vasoconstriction. The limited research encourages the critical care nurse to investigate the available patient population in terms of oxygenation and tissue perfusion. It is certainly clear that nursing interventions should focus on assessing and planning care of these patients in view of the individual's oxygen delivery and oxygen consumption responses to therapeutic measures.

Chapter 5

Physiological Factors Preventing Optimal Functioning of Vasoactive Drugs

Adequate oxygen transport depends on a number of parameters including a PaO2 of at least 60 mm Hg, normal cardiac output, normal hemoglobin levels and normal metabolic demands with healthy cellular functioning (Rutherford, 1989; Reischman, 1988). Failure to maintain these conditions can limit oxygen delivery thus limiting oxygen consumption in spite of the best pharmacological interventions. Lung failure, cardiac failure, hemorrhage, an inability of hemoglobin to release oxygen, increased metabolic needs or the inability of cells to utilize oxygen will all reduce oxygen delivery to and/or consumption by the cells (Schumacker & Cain, 1987).

Oxygen must find its way from inspired air to the alveoli then onto hemoglobin and eventually to the tissues and into the cells. A breakdown in any of these areas will preclude adequate tissue oxygenation. An in depth review of all the factors which can prevent adequate tissue oxygenation is beyond the scope of this paper. However, ventilation/perfusion (V/Q) mismatches, shifting of the oxyhemoglobin dissociation curve and the impact of oxygen free radicals will be discussed.

Ventilation/Perfusion Mismatches

A variety of situations can alter gas exchange starting with the amount of oxygen which is inspired. Other conditions include alveolar hypoventilation, defects in carbon dioxide and oxygen's ability to diffuse across the membrane, ventilation and perfusion mismatches and intrapulmonary shunting (Rutherford, 1989; Von Rueden, 1989; Reischman, 1988; Schumacker & Cain, 1987).

Alveolar hypoventilation occurs when alveoli are not adequately ventilated. Carbon dioxide further accumulates in the alveoli. There are numerous causes for this dysfunction. Among the most common causes are chronic obstructive pulmonary disease and central nervous system dysfunction including spinal cord and brain injuries (Von Rueden, 1989; Reischman, 1988).

Diffusion defects affect the alveoli and capillary membranes. These defects impact on the ability of carbon dioxide to move from the unoxygenated blood into the alveoli for expiration and affects the movement of oxygen from the alveoli into the pulmonary venous blood. Diffusion defects are seen in patients with pulmonary fibrosis and adult respiratory distress syndrome among others (Von Rueden, 1989; Reischman, 1988).

A knowledge of ventilation of alveoli and perfusion within the normal lung is needed to understand V/Q mismatching.

Ventilation does not occur evenly throughout the lung. The dependent portion of the lung is ventilated to a larger extent then the upper portion of the lung (West, 1990; Reischman, 1988; Weibel, 1984). Perfusion follows ventilation. Therefore, the dependent portion of the lung is better perfused then the upper portion of the lung (West, 1990; Hoyt, 1988; Reischman, 1988; Weibel, 1984). The dependent portion of the lung may be the base of the lung if the individual is sitting or the posterior or anterior portion of the lung if the individual is laying supine or prone.

Alveolar and capillary pressures also affect ventilation and perfusion. Alveolar pressure remains constant throughout the lung. Alvoloar pressure pushes against the capillaries limiting blood flow through the capillary. As capillary pressures increase, blood flow is enhanced. At the apices of the lung, alveolar pressure is greater than capillary pressure, therefore, blood flow is limited. Arterial pressure exceeds alveolar pressure during systole in the middle region of the lung. This increase in arterial pressure opens up additional capillaries in this region, enhancing blood flow to the region. The lower region of the lung has pulmonary capillary pressures which are higher than the alveolar pressure, thus providing the normal

impetus for perfusion (West, 1990; Reischman, 1988; Guyton, 1986; Weibel, 1984).

The changes in capillary pressures ensure that ventilation and perfusion conditions are not constant in a normal lung. An abnormally high V/Q ratio occurs where ventilation is greater than perfusion such as in the apices of an individual sitting upright. An abnormally low V/Q ratio occurs when perfusion exceeds ventilation, such as in the bases of the lungs of an individual sitting upright (West, 1990; Reischman, 1988; Weibel, 1984).

When alveoli are hypoventilated, the normal lung responds in a compensatory manner to prevent V/Q mismatching. The capillaries near hypoventilated alveoli constrict, thus shunting blood away from hypoxic alveoli. The constriction of these capillaries is referred to as hypoxic pulmonary vasoconstriction. By reducing blood flow to the hypoventilated alveoli, normal V/Q ratios are restored to that area. Hypoxic pulmonary vasoconstriction also encourages enhanced blood flow to the better ventilated alveoli. This allows for optimal gas exchange and enhanced oxygen delivery (West, 1990). Vasodilators have been demonstrated to override this compensatory mechanism thus

causing physiologic shunting within the lung (Mollhoff et al., 1990; Mookherjee et al., 1977).

Shunting occurs when a portion of the stroke volume remains unoxygenated. There is either decreased ventilation in relation to perfusion, or decreased perfusion in relation to ventilation when this occurs. A normal physiologic shunt occurs from the blood flow of the bronchial, pleural and thebesian veins which empty directly into the arterial circulation. This shunt is approximately 2 - 5% of the cardiac output. Shunts less than 10% are considered within normal range. Noncritical pulmonary abnormalities are identified with shunt levels of 10 - 19%. Very serious pulmonary abnormalities are noted at shunt levels of 20 - 29%. Life threatening V/Q abnormalities are seen at shunt levels of 30% or more (Von Rueden, 1989; Reischman, 1988).

Shunts are separated into three categories. The first is anatomical shunting where blood does not come into contact with oxygen. A pathological example of this is right - to - left intracardiac shunts. Oxygen therapy does not help reduce this shunt because the alveolar gas does not come in contact with this blood flow. A second type of shunt is the capillary shunt. Blood flow in this shunt moves past alveoli; however, the alveoli are unventilated. Some pathological causes for this type of

shunt are atelectasis or fluid-filled alveoli. The third shunt is known as a venous admixture shunt. Perfusion is greater then ventilation in the presence of this shunt; however, some ventilation of the alveoli exists. Alveolar hypoventilation and excessive perfusion are causes of venous admixture shunting (Rutherford, 1989; Von Rueden, 1989; Reischman, 1988).

Understanding V/Q mismatches and types of shunt are important when assessing a patient's oxygenation and tissue perfusion status. Efforts to increase tissue perfusion will be useless if the elevated cardiac output is full of unoxygenated blood related to a physiologic shunt. If a shunt is present, enhanced cardiac output will not increase oxygen delivery to the tissues. In this case, efforts must be made to intervene at the shunt site allowing for increased oxygen in the alveoli and appropriate pulmonary gas exchange. The nurse must assess the patient's V/Q ratio to determine if adequate pulmonary gas exchange is taking place. This is especially important for patients receiving vasodilators as hypoxic pulmonary vasoconstriction may be inhibited and increased perfusion may take place in areas of alveolar hypoventilation.

Shift of Oxyhemoglobin Dissociation Curve

A second area of concern, which can prevent optimal functioning of vasoactive drugs, is the ability of oxygen to dissociate from hemoglobin and move into the cells. Each hemoglobin molecule has the ability to bind four oxygen molecules to the heme portion of its configuration. The affinity of oxygen to hemoglobin is reflected by the arterial saturation of oxygen. This affinity is reversed at the cellular level allowing oxygen to be released to the cells. The oxyhemoglobin dissociation curve depicts the oxyhemoglobin relationship (West, 1990; Mims, 1989; Von Rueden, 1989; Hoyt, 1988; Weibel, 1984).

Oxyhemoglobin affinity can be increased or decreased, depending on the patient's status, and in some cases, the medical team's interventions. A decrease in affinity, or a shift to the right of the oxyhemoglobin curve, allows for an easier release of oxygen to the cells. Causes of decreased oxyhemoglobin affinity include acidosis, hypercapnea, hyperthermia and increased levels of 2,3 - diphosphoglycerate (2,3 - DPG) (Mims, 1989; Von Rueden, 1989; Hoyt, 1988; Weibel, 1984).

An increase in oxyhemoglobin affinity is represented by a shift to the left on the oxyhemoglobin dissociation curve. This shift reduces oxygen's release to the cells. Even though there

is adequate oxygen in the cardiac output, the oxygen molecules cannot move into the cell. This shift to the left prevents oxygen delivery to the tissues. Causes of an increased oxyhemoglobin affinity include alkalosis, hypocarbia, hypothermia, hypophosphatemia and decreased levels of 2,3 - DPG (Mims, 1989; Von Rueden, 1989; Hoyt, 1988; Weibel, 1984). A decreased level of 2,3 - DPG is especially important to consider when a patient receives several units of banked blood. Hypothermia may also be a problem to consider, as banked blood is both cold and deficient in 2,3 - DPG (Mims, 1989; Von Rueden, 1989).

A patient with an adequate arterial saturation may have difficulty releasing oxygen at the cellular level. Causes of an increase in oxyhemoglobin affinity should be considered and assessed. Vasoactive drugs will not impact oxyhemoglobin affinity and therefore will not return the oxyhemoglobin dissociation curve to normal. This is especially important if it is shifted to the left, preventing oxygen release to the cells. This is a situation where enhanced oxygen delivery does not allow for enhanced oxygen consumption as the oxygen cannot be released to the cells.

Oxygen Free Radicals

Increased oxygen delivery and the ability of hemoglobin to release oxygen at the cellular level is useless if the cell cannot extract and use the oxygen. Everyday responses to tissue injury, inflammation and bacterial invasion can initiate a crisis for the critically ill patient. The activation of complement, coagulation and certain enzyme systems bring about a release of mediators which eventually do cell damage and lead to the production and release of oxygen free radicals (Baue, 1990; Bulkley, 1983).

Oxygen free radicals pose a threat to cell integrity and may prevent the cell from accomplishing its tasks, including the consumption of oxygen. Lysosome and mitochondria disruption may occur in the presence of an overabundance of oxygen free radicals. Small amounts of oxygen free radicals are phagocytic and, therefore, are healthy. In fact, the normal oxygen reduction process leaks 1 - 2% of oxygen free radicals. A usual response to this leak is the presence of a small amount of superoxide detoxifiers which prevent the normal amount of oxygen free radicals from becoming threatening (Baue, 1990; Bulkley, 1983).

A critically ill patient experiences a large release of oxygen free radicals through a variety of cascades. The activation of phagocytes and neutrophils, produced by these cascades, initiates the formation of oxygen free radicals (Baue, 1990; Fantone, 1990). Additionally, oxygen free radicals produce a chain of events which cause a further release of oxygen free radicals magnifying the negative effect of oxygen free radicals on the body. This cascade of events is initiated by a large variety of clinical events making all critically ill patients susceptible to this dilemma. These clinical situations include inflammation, tissue injury, ischemia especially with reperfusion injury, shock states, hyperoxygenation syndromes, radiation therapy and aging (Baue, 1990; Bulkley, 1983). Hypothesized areas of concern include patients who smoke, have emphysema or atherosclerosis (Baue, 1990).

Once a clinical situation develops, tissue injury for example, the cascade of events can occur. Enzyme cascades, activated with tissue injury or in response to the threat of infection, include the renin-angiotension-aldosterone cascade, the coagulation cascade, the fibrinolysis cascade, the kallikrein-kinin system, the complement cascade and the arachidonic acid cascade. Each of these cascades have normal

physiological functions within the body. They also have pathological responses which begin the oxygen free radical cycle within the body (Baue, 1990).

The renin-angiotension-aldosterone cascade normally promotes sodium retention. Enhanced activation of this cascade prevents the diuresis of excessive volume. The coagulation system normally provides homeostasis. Intravascular coagulation occurs which prevents normal blood flow when excessive activation of the coagulation system occurs. The fibrinolysis cascade destroys intravascular fibrin and clots normally and, when overactivated, predictably causes abnormal bleeding. The complement system normally provides opsonization for phagocytosis of bacteria, damages or lyses specific cells or tissues and promotes inflammation. This cascade causes neutrophil activation and aggregation, and the release of a variety of mediators from C3a and C5a in a pathological state.

The arachidonic acid cascade splits into two separate cascades. The first cascade is the cyclooxygenase pathway which metabolizes into prostaglandins. Normally, prostacyclin and PGE2 inhibit aggregation, stabilize membranes and vasodilate vessels. Excessive stimulation encourages thromboxane and PGF2a to constrict vessels and promotes aggregation of leukocytes and

platelets. The second pathway off the arachidonic acid cascade is the lipoxygenase pathway. This pathway metabolizes arachidonic acid into leukotrienes which normally contribute to the inflammatory response. Excessive leukotriene production increases the permeability of the vessels, promoting capillary leakage which can lead to edema (Baue, 1990).

The interrelationship of these cascades provides the impetus for further enlargement of oxygen free radical damage. Beginning with the coagulation cascade, an association is seen with arachadonic acid. Homeostasis, as a product of the coagulation system, is divided into two components. Primary homeostasis occurs through the use of platelet plugs. Platelet activation is caused by a number of components. Arachidonic acid release, as well as other biochemical events, is involved in this platelet activation. Secondary homeostasis consists of fibrin formation, which strengthens the platelet plug. The relationship between the coagulation cascade and the inflammatory response is apparent as fibrin is often deposited in response to the inflammatory system's activation of phagocytes and macrophages (Baue, 1990).

The complement system has a classical pathway and an alternate pathway. Anitgen-antibody substances initiate the classical complement pathway while bacterial products and toxins

initiate the alternate complement pathway. Both pathways ultimately cause C3a and C5a to release mediators which cause degranulation of mast cells, basophils and neutrophils. Neutrophils are responsible for respiratory bursts. These bursts are actually oxygen-dependent biochemical events which produce oxygen free radicals. These toxic substances are normally an antimicrobial response. Excessive neutrophil activation causes an increased amount of oxygen free radical production which then damages the normal cells (Baue, 1990). This decreases the cell integrity and prevents oxygen consumption from occurring.

The kallikrein-kinin system is also intertwined with the complement and coagulation cascades as well as the inflammatory response. Any clinical situation which activates the coagulation cascade initiates the kallikrein-kinin system as Factor XII (the Hageman Factor), of the coagulation cascade, activates the kallikrein-kinin system. The kallikrein-kinin system then activates Factor XI of the coagulation cascade thereby promoting clotting. Bradykinin is a result of this system and may be a mediator for the inflammatory response. Complement is activated causing C3a and C5a to release their anaphylatoxins causing oxygen free radical production (Baue, 1990).

Arachidonic acid is released when cell membranes are disturbed. It is a free fatty acid that is a precursor for leukotrienes, metabolized from the lypoxygenase pathway, as well as prostaglandins and thromboxane, via the cyclooxygenase pathway. The overall effects of these eicosanoids include changing cell membrane permeability, vasodilation and vasoconstriction, chemotaxis, platelet aggregation and white blood cell aggregation. The cell membrane damage further stimulates the mediator pathways and allows neutrophils to continue producing oxygen free radicals which cause greater damage (Baue, 1990).

Enhancing oxygen delivery, when this process is occurring at the cellular level, will not increase oxygen consumption. Vasoactive drugs alone will not promote the needed oxygen-carbon dioxide exchange at the cellular level. Efforts must be made to stop the mediator pathway cycle while optimizing other therapeutic interventions, including the use of vasoactive drugs.

Summary

Oxygen consumption is enhanced by increased oxygen delivery in critically ill patients. Vasoactive drugs manipulate cardiac output to provide an increase in oxygen delivery. However, this

is not a consistent change. Each patient must be assessed on an individual basis to ensure optimal functioning of these drugs.

The desired outcome for the critically ill patient is an enhanced oxygen delivery allowing for an increase in oxygen consumption to meet the increased oxygen demands of the body. Vasoactive drugs may not increase oxygen consumption for a variety of reasons. This limited discussion of V/Q mismatches, intrapulmonary shunting, shifting of the oxyhemoglobin dissociation curve and oxygen free radical production provides a background of areas which should be assessed if oxygen consumption is not increased with enhanced oxygen delivery.

Chapter 6

Implications for Advanced Nursing Practice

Vasoactive drugs are used, when available, to provide the best medical care possible for all types of critically ill patients. Vasoactive drugs are useful medical interventions when caring for patients with such pathological processes as septic shock, myocardial infarction, hypertension and hypotension and for patients requiring such procedures as open heart surgery patients. Certainly this list is incomplete. The use of vasoactive drugs spans the spectrum of critical care illnesses and intensive care units. The use of these drugs may be implemented in the Emergency Department setting as easily as in the intensive and progressive care settings. Nurses in all areas must be prepared to care for critically ill patients receiving vasoactive drugs.

An important part of this nursing care is the assessment of the patient receiving vasoactive drugs (Burns, 1990). The Clinical Nurse Specialist (CNS) has the responsibility of ensuring that nurses are able to accomplish a thorough assessment of this patient. Therefore, the CNS must demonstrate expert clinical knowledge, anticipating the patient's response to any nursing or medical intervention. The CNS must be able to assess

a given clinical situation, provide an appropriate plan of care based on their clinical judgement, implement this plan of care, explaining the reasons for the nursing actions and evaluate the patient outcomes (Spross & Baggerly, 1989). Additionally, the CNS must fulfill the responsibilities of the other subroles of advanced nursing practice including consultant, educator and researcher.

Clinical Expert

The primary function of the CNS is as a clinical expert practitioner (American Association of Critical-Care Nurses, 1989). The clinical expert role can be divided into two subcategories; direct and indirect patient involvement. Direct patient involvement allows the CNS to act as a role model, providing excellent care for both the patient and family. Indirect involvement in patient care provides the CNS with the opportunity to collaborate with the nurse/physician team and facilitate the staff nurse in providing optimum patient care (Koetters, 1989).

As a clinical expert providing direct patient care, the CNS must demonstrate the most comprehensive techniques for assessing the patient receiving vasoactive drugs. Assessment of these patients must focus on oxygen delivery and oxygen consumption

parameters. The goal for vasoactive therapy in both the Emergency Department and ICU setting is ensuring oxygen delivery and optimizing oxygen consumption for the individual.

The Emergency Department CNS may not have the benefit of pulmonary artery catheter measurements. Advanced schooling enables the CNS to understand that the assessment must focus on level of consciousness, urine output, color, temperature and pulses of the extremities and monitoring for complaints, signs and symptoms associated with myocardial ischemia, heart rate and blood pressure (Burns, 1990). Evaluation of these parameters enables the CNS to determine changes in oxygen delivery and tissue perfusion. The CNS acts as a role model for the staff nurse, documenting the data and evaluating the patient outcome based on the therapeutic interventions. Titration of the drugs as well as other changes in the therapeutic interventions are made based on these patient outcomes.

The Intensive Care CNS provides the same expert care, acting as a role model for the Intensive Care Unit (ICU) Staff Nurse. However, the ICU CNS must also be prepared for the advanced technology used in this area. This technology includes the ability to observe and assess for changes in hemodynamic parameters. Patients receiving vasoactive drugs may have

volatile hemodynamic parameters requiring rapid nursing interventions. The ICU CNS must be prepared to implement changes, providing rationale for the modification in therapy.

CNS clinical experts involved with indirect patient care focus on two aspects, the staff nurse the patient care process (Koetters, 1989). An important part of indirect patient ca: a CNS provides is the development, implementation and evaluation of standards for critical care nursing practice (American Association of Critical-Care Nurses, 1989; Koetters, 1989). Standards of practice provide a reference for nurses who are delivering care to patients receiving vasoactive drug therapy (Clark & Garry, 1991).

The Standard of Practice for Vasoactive Drug Therapy, developed by the CNS, should include assessment techniques specific for patient assessment, as previously outlined, as well as hemodynamic parameter assessment minimally including cardiac output, systemic vascular resistance, pulmonary artery diastolic pressure, pulmonary artery wedge pressure, oxygen consumption, oxygen extraction (Burns, 1990). A plan for implementing the therapy should also be included indicating the use of a central venous site for access, an infusion pump, specific types of tubing and fluid, as necessary. The CNS must ensure standards of

practice are based on findings in the literature, including medical and nursing research (Clark & Garry, 1991).

Consultant

The CNS acts as a consultant on both a formal and an informal basis. Additionally, the CNS may have preordained rounds or meetings for discussion of referrals (Barron, 1989). As a consultant, the CNS utilizes all of the identified CNS subroles to provide expertise to the health care provider and health care consumer. The CNS consultant, using the nursing process, applies change theory enabling the consultee to make a decision and plan for implementation of that decision (Emergency Nurses Association, 1991; American Association of Critical-Care Nurses, 1989).

The use of vasoactive drugs requires collaboration between health care team members. The CNS may assist the medical provider in understanding nursing standards of practice associated with vasoactive drug therapy. For instance, access through a central line to prevent peripheral tissue damage may be noted in the standard of practice. However, a physician must place the central line. Pharmacist input provides current research and clinical data which can impact nursing standards of practice. Collaborating on the standards of practice encourages

joint decision-making, and the dissemination of the decisions to all members of the health care team.

The CNS may act as a consultant to the health care team for establishing protocols which integrate vasoactive drug therapy with other medical interventions for specific disease processes. For example, the integration of vasoactive drug therapy, oxygenation, fluids, antibiotics and nutrition vary for patients with septic shock as opposed to patients undergoing open heart surgery (Burns, 1990). The Cardiovascular CNS and the Trauma CNS may act as consultants, establishing protocols appropriate for each nursing area.

The CNS also acts as an informal consultant, responding to the needs of the patient, family and/or the staff nurse at the bedside. The indications for vasoactive therapy differ for each patient. A nurse, unfamiliar with the intricacies of vasoactive drugs, may require the clinical expertise of the CNS to solve a problem or understand a plan of care. Reinforcing the goals of enhanced oxygen delivery and optimal oxygen consumption for nurses new to the critical care setting becomes an important part of the CNS informal consultant role.

The CNS may consult with the patient's family, creating ways to assist the patient's family in understanding the disease

process and the care being provided. The understanding the family achieves with this reinforcement of factual information regarding the patient's condition may help the family maintain hope during a critically ill patient's changing course (Leske, 1991; Simpson, 1989).

Educator

The CNS subrole of educator encompasses the nursing staff, the patient and their family. The focus of the CNS educator is on patient care. This focus differentiates the CNS educator from other nurse educators whose focus is on education. There are three aspects of staff education requiring the CNS educator's attention. These are orientation of the staff, in-services and continuing education offerings. The patient and family educational needs are more complex, requiring innovative interventions from the CNS educator. The goal for patient and family education is to gain an understanding of the patient illness, the hospital course and the implications of the illness based on patient and family needs (Priest, 1989).

Staff education of vasoactive therapy begins in the orientation process. The CNS educator must establish the goals of the education process with regards to vasoactive therapy. Competency for administering vasoactive drugs differs from the

competency for administering antibiotics because of the different actions and nursing interventions of the drugs. Vasoactive drug competency may focus on the route of administration, the goals of patient care, and the need for titration to maintain an optimal environment for the patient.

However, staff competency requires more than the ability to understand the indications and mechanisms of action for vasoactive drugs. Staff competency also requires more than the ability to mix the drug and initiate the intravenous infusion. Demonstration of staff competency for administering vasoactive drugs must include an evaluation of the performance in a given clinical situation, thereby assessing the staff's actions in providing competent vasoactive drug therapy. The nurse must be able to integrate the needs of the patient with the actions of the drug, provide a comprehensive assessment, and change nursing interventions based on clinical judgement, supported by research, which the staff member describes (Alspach, 1992). The CNS educator, because of his/her clinical expertise and knowledge of the clinical situation, is best able to provide the standards for this evaluation criteria (Priest, 1989).

The CNS educator must contribute to the nursing knowledge base of vasoactive drug therapy through the presentation and

publication of scholarly works (Emergency Nurses Association, 1991; American Association of Critical-Care Nurses, 1989). Case studies are often beneficial as they facilitate the integration of knowledge. A case study approach allows the learner to direct the learning. This approach motivates the learner to higher levels of achievement including integration and application of knowledge, which allows for competency-based education to occur (Alspach, 1992; Echols, 1984).

A collaborative effort between the Emergency Department CNS, the ICU CNS and the Pharmacist would facilitate a higher level of integration of vasoactive drug therapy knowledge. This cooperative venture could help define the roles and actions of the Emergency Department nurse in the initiation of vasoactive therapy. The indications for vasoactive therapy, the assessment of the patient and the nursing interventions change as the patient is moved from the Emergency Department to the ICU setting, although the goal of the therapy remains the same, that of increased oxygen delivery and optimal oxygen consumption. An integration of one patient moving through the medical system provides an opportunity to assess and improve the continuity of patient care. The CNS educator offers these experiences, thus working to enhance the patient care system.

Researcher

Publishing scholarly works is an excellent way to broaden nursing knowledge. To further this effort, an important subrole of the CNS, researcher, dictates that the CNS become involved in research opportunities. Research involvement includes conducting research, facilitating research and applying research to the clinical setting. The CNS researcher must disseminate research findings, including both presentation and publication of the research project. Publicizing research studies and the conclusions reached by the investigators expands the scientific basis of nursing. Nursing knowledge can then be *reinforced* (Emergency Nurses Association, 1991; American Association of Critical-Care Nurses, 1989; McGuire & Harwood, 1989). Unit protocols, frequently written or reviewed by the CNS, should be based on research findings (Clark & Garry, 1991).

To date, nursing has shown limited involvement in research projects which study the impact of vasoactive drugs on the body's oxygen delivery and oxygen consumption. Nurses work at the patient's bedside, constantly assessing the patient's oxygenation and tissue perfusion. Conducting research which studies the effect of these drugs, administered by nurses, on a patient's oxygenation and tissue perfusion is within the realm of nursing

research. Research questions could include assessing the impact of any vasoactive drug on oxygen delivery and consumption. Studies could be conducted using specific patient populations with specific pathological processes. What is the impact on the pediatric population receiving vasoactive drugs? What is the impact on the geriatric population receiving vasoactive drugs? What impact does the loss of hypoxic pulmonary vasoconstriction have on the body's total oxygen delivery and consumption? Are there nursing interventions that are required when hypoxic pulmonary vasoconstriction is lost? How are patient outcomes affected through the use of vasoactive drugs?

The CNS has a responsibility to encourage research on the unit through an enthusiastic approach to the possibilities of research. Advanced education and clinical expertise enable the CNS to conduct and/or facilitate research in the clinical setting. Because of the varied uses of vasoactive drugs, a collaborative approach should be used during some research projects. For example, the impact of initiating vasoactive therapy at the earliest possible time on patient outcome could be a collaborative study between Emergency Department and ICU personnel in conjunction with the medical providers and pharmacists.

The CNS research should focus the research project, making it a manageable study for data collection and analysis purposes. Advanced education, and networking with other CNS's provides the guidance needed to accomplish a thorough data analysis. The use of local university and in-house computer systems eases the strain of this complex process. The CNS research must make research approachable to the staff nurse. Enthusiasm and dedication from the CNS empowers the staff nurse to conduct, participate in and utilize research in the clinical setting.

Summary

The implications of the advanced nurse practitioner subroles demonstrates the need for continued encouragement of the CNS position. The clinical expert challenges the bedside nurse to achieve excellence when caring for the critically ill patient receiving vasoactive drug therapy. Acting as a consultant to the patient's family and supporting them at this time of crisis offers them a realistic view of the patient's course of stay. The researcher must be an important contributor to future discoveries of uses and nursing implications for vasoactive drug therapy. Ultimately, the CNS facilitates growth and development in himself or herself, as well as in other members of the health

care team, the patient and the patient's family through the use of clinical expertise, consulting, education and research.

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